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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,130	11/27/2001	David B. MacLean	PC11088ATMC	9834

7590 06/03/2004

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EXAMINER

WANG, SHENGJUN

ART UNIT PAPER NUMBER

1617

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/995,130

Applicant(s)

MACLEAN, DAVID B.

Examiner

Shengjun Wang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 61 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 3/7/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 17, 2004 has been entered.

Claim Rejections 35 U.S.C. 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacLean et al. (USPN 5,889,042) and Lund et al. (Testosterone and andropause, Pharmacotherapy 19 (8):951-6, August 1999).

4. MacLean et al. (USPN 5,889,042) teaches a method of treating testosterone insufficiency employing (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8-tetrahydronaphthalen-2-ol, the elected specie herein. Administering the compound to elderly men result significant increase of testosterone level. See, particularly, the abstract, column 2, line 40 to column 5, line 41, and column 34, lines 15-57. Lund et al. teaches that elderly men suffering from andropause with low levels of testosterone benefited from a testosterone replacement therapy, see abstract and page 953 in particular. Lund et al. further teaches that steadily declining circulating testosterone levels in men suffering of andropause are implicated as a potential cause

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of symptoms and that restoring testosterone to physiological levels ameliorates symptoms associated with andropause.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ both (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8-tetrahydronaphthalen-2-ol, and testosterone in a method of treating andropause. One of ordinary skill in the art would have been motivated to employ both (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8-tetrahydronaphthalen-2-ol, and testosterone in a method of treating andropause because employing two agents that are individually known to be useful in treating andropause in a method of treating the same is prima facie obvious. The Skilled Artisan would reasonably expect to obtain an additive effect by combining the two agents. Further, it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus, the claimed invention which is a combination of two agents known for treating testosterone deficient, sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

5. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over MacLean et al. (USPN 5,889,042) and Lund et al. "Testosterone and andropause," Pharmacotherapy 19 (8):951-6, August 1999), of reasons discussed above, and in further view of Chiu et al. (US 5,948,809, IDS).

6. MacLean and Lund do not teach expressly the tartrate salt of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8-tetrahydronaphthalen-2-ol. However, Chiu et al. teaches that tartrate salt of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8-

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tetrahydronaphthalen-2-ol is a pharmaceutical acceptable salt of tartrate salt of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8- tetrahydronaphthalen-2-ol. See, particularly, the abstract and the claims.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to use the tartrate salt of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8- tetrahydronaphthalen-2-ol as a pharmaceutical acceptable salt since tartrate salt of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8- tetrahydronaphthalen-2-ol is a known pharmaceutical acceptable salt of (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-s,6,7,8- tetrahydronaphthalen-2-ol.

Response to the Arguments

Applicants' amendments and remarks submitted March 17, 2004 have been fully considered, but are not persuasive.

In response to applicants' arguments that MacLean did not teach treating andropause as herein claimed, one of ordinary skill in the art would understand that testosterone is one of the symptoms of andropause, treatment of a symptom are considered treatment of a syndrome with the symptom. The argument that some of the testosterone deficient patients are not andropause is not relevant. Men with andropause are deficient in testosterone. See, page 952 in Lund.

Applicants contend that exogenous testosterone would inhibit the production of endogenous testosterone, therefore there is no reasonable expectation of success. Such arguments are not probative. Particularly, What Fujioka disclosed merely showed that normal young men could somehow maintain the testosterone level even with the extra intervenes. Nowhere in Fujioka are testosterone deficient elder men ever discussed. One of ordinary skill in the art would


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have not expected testosterone deficient elder men to be the same as the young men with respect to the ability to maintain the level of testosterone. Further, MacLean proved the particular estrogen agonist/antagonist are useful for increasing the level of testosterone in elder men whose level of endogenous testosterone are suppressed, such estrogen agonist/antagonist would have been expected to be effective to overcome suppression of endogenous testosterone. Therefore, the combination of the particular estrogen agonist/antagonist and testosterone would have been reasonably expected to be useful for increasing the level of testosterone.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9302.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

 **SHENGJUN WANG**
PRIMARY EXAMINER

Shengjun Wang

May 30, 2004